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09/582,809	06/30/2000	GEORGE E. SEIDEL	XY-LODO-USNP	3161
33549 7590 07/21/2008 SANTANGELO LAW OFFICES, P.C. 125 SOUTH HOWES, THIRD FLOOR FORT COLLINS, CO 80521			EXAMINER MYERS, CARLA J	
			ART UNIT	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b> 09/582,809	<b>Applicant(s)</b> SEIDEL ET AL.	
	<b>Examiner</b> Carla Myers	<b>Art Unit</b> 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 28 March 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 186-194, 196, 197, 199-203, 205-208, 210-216 and 219-227 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 186-194, 196, 197, 199-203, 205-208, 210-216 and 219-227 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Applicant's arguments and amendments set forth in the response of March 28, 2008 have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn.

This action is made FINAL.

2. Claims 186-194, 196,197, 199-203, 205-208, 210-216 and 219-220 and newly added claims 221-227 have been examined herein.

### **Terminal Disclaimer**

3. The terminal disclaimer filed on March 28, 2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 7,195,920 and any patent that issues from U.S. Application No. 09/744,675 and 10/081,955 has been reviewed and is accepted. The terminal disclaimer has been recorded.

### **New Grounds of Rejection**

#### **Claim Rejections - 35 USC § 112**

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 221-227 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not provide support for the amendment to add new claims 221-227. In particular, the specification does not provide support for the concept recited in claim 221, and dependent claims 222-227 of a methods wherein fertilization of a female egg occurs at success levels statistically comparable to an unsorted artificial insemination sample having about an equal number of sperm cells. The response of March 28, 2008 points to Example 1 of the specification as providing support for this amendment. However, Example 1 does not in fact provide support for this concept. The specification also does not provide support for the use of "no more than about 350,000 of said sorted sperm cells" (claim 221, step "f"). While the originally filed specification provides support for the concept of providing an insemination sample comprising "no more than three hundred thousand sperm", the specification does not appear to provide support for the broader concept of an insemination sample comprising "no more than about 350,000 sorted sperm." Further, the specification does not provide support for the recitation that insemination occurs at "about 5 hours following said step of sorting" (claim 222) or "no more than about 9 hours following said step of sorting." The specification (page 25) provides support only for the concept that insemination occurs "5 to 9 hours after sorting." The specification also does not provide support for the concept of inseminating a female "no more than about 6 hours following observed standing estrus" (claim 225) or "no more than about 26 hours following observed standing estrus" (claim 226). The response points to Example 1 as providing

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support for these recitations. However, Example 1 (page 25) provides support only for the concept of performing insemination 6-26 hours after observed standing estrus.

Regarding claim 227, the specification does not provide support for the recitation of “at least 5 degrees Celsius.” Again, the response points to Example 1 as providing support for this recitation. However, Example 1 (page 25) discloses only the concept of cooling the artificial insemination sample to 5 degrees Celsius and transporting straws at 3 to 5 degrees Celsius.

### **Maintained Rejections**

5. The following grounds of rejection were previously presented in the Office action of September 28, 2007 and have been modified to address the claims as amended in the response of March 28, 2008.

### **Claim Rejections - 35 USC § 103**

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 186-189, 191-194, 196-197, 202, 208, 213-216, 219 and 221-227 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (Journal of Animal Science. July 1996, 71 (supplement 1) abstract 513 "Insemination of heifers with very low numbers of frozen spermatozoa"; cited in the IDS) in view of Seidel (Theriogenology. January 1996. vol. 45, page 309; cited in the IDS) and Rens (U.S. Patent No. 5,985,216).

Seidel (July 1996) teaches methods comprising collecting semen from a male bovine, extending the semen in homogenized milk with 7% glycerol extender plus 5% homologous seminal plasma to obtain an artificial insemination sample containing 2 or  $5 \times 10^5$  total sperm per 0.25ml straw, freezing the artificial insemination sample, thawing the sample to ambient temperature, inseminating synchronized female heifers by inserting half of the semen sample deep into the uterine horns and fertilizing at least one egg within said bovine. Seidel teaches that the method using  $5 \times 10^5$  total frozen/thawed sperm (i.e., a "low number" of sperm) achieved fertilization success rates "statistically comparable" to that obtained using a typical insemination dosage (i.e.,  $10 \times 10^6$  total sperm/inseminate).

Seidel (July 1996) does not teach sorting the sperm prior to artificial insemination.

However, Seidel (Jan 1996) teaches methods for making bovine mammals comprising sorting sperm cells according to sex using flow cytometry wherein the sperm cells are sorted to purity rates of about 90%, establishing an insemination sample, inserting a low dosage ( $1-2 \times 10^5$  in .1 ml) of sorted sperm cells into the uterine horns of

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the female bovine after the onset of estrus; and fertilizing the eggs of the bovine so as to produce at least one offspring of the desired sex. Seidel teaches that 11 of 22 females inseminated with sperm cooled to 5°C during shipping were pregnant at 8 weeks. The sperm were deposited deep in the uterine horn ipsilateral to the ovary with the largest follicle being determined by ultrasound.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel (July 1996) so as to have sex sorted the sperm as taught by Seidel (Jan 1996) prior to artificial insemination in order to have provided an effective means for controlling the sex of the bovine offspring.

Further, Seidel (July 1996) and Seidel (Jan 1996) do not teach sorting sperm at rates of 1200 sorts/second.

However, Rens teaches a method of sex-sorting sperm using high speed flow cytometry. In the method of Rens (see columns 4-6), a sample of sperm is obtained from a male mammal, the sperm is stained with Hoechst 33342 dye in order to distinguish between viable and nonviable sperm (column 5, lines 4-10), the sperm are sorted in a high speed flow cytometer using a nozzle that forms a stable droplet containing each individual sperm cell (column 2, lines 23-32), the sperm are sorted according to their sex characteristics and isolated populations of X- and Y-chromosome bearing sperm are collected. Importantly, Rens (col. 5) discloses modifying the MoFlo® high speed cell sorter to include a new elliptical nozzle capable of more accurately orienting sperm for accurate sorting. Rens teaches use of the modified MoFlo® sorter using sampling rates of 500 sperm/second and 2000 sperm/second (column 6). Further,

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Rens teaches that the modified MoFlo® sorter also allowed for sample rates up to at least 15,000 sperm/sec (column 4, lines 29-31). Rens (col. 2) teaches that the flow cytometry apparatus disclosed therein provides for improved accuracy and efficiency of sorting, as compared to prior art flow cytometers. Rens (col. 2) also discloses the motivation to use high speed cell sorters to maximize the number of sorted sperm per unit time. For example, Rens (col. 4) discuss the requirement to use large quantities of sperm for artificial insemination and states that by using the high speed cell sorter equipped with the nozzle disclosed therein, the yield of sex sorted sperm cells can be increased at least 10 fold, making artificial insemination with sexed semen a more feasible option. Rens (col. 7) also exemplifies a method wherein a total of 50 million X and Y sperm were sorted in a 7 hour period using the modified MoFlo® sorter equipped with the new elliptical nozzle.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel so as to have used high sorting rates, including sorting rates of about 500 sorts /second or 1200 sperm/second, in order to have allowed for the faster sorting of sperm so as to have provided adequate quantities of sex-sorted samples that could be used for the insemination process. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). Further, It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the



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art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious). In the present situation, the prior art teaches provides the motivation to increase sort speeds to at least 1200 sperm/sec and the means for achieving this result (i.e., the modified MoFlo® high speed sorter including the elliptical nozzle of Rens). Thereby, modification of the method of Seidel to use the high speed sorter of Rens to sex-sort sperm cells at rates of 500 sorts/sec or 1200 sorts/sec would have been obvious to one of ordinary skill in the art and well within the skill of the art at the time the invention was made.

Regarding claim 187, Seidel (July 1996) teaches applying the method to bovine.

Regarding claim 188, Seidel (July 1996) teaches that the method is performed under field conditions.

Regarding claim 189, Seidel (July 1996) does not specifically teach repeating the process in a "significant number" of females in a farm or ranch condition. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have repeated the method of Seidel with additional female bovine in "farm or ranch conditions" in order to provide an effective means for inseminating female bovine under natural conditions to produce a large number of bovine offspring.

Regarding claims 191-194, Seidel (July 1996) teaches inserting the semen deep into each uterine horn using an embryo transfer gun (i.e., "embryo transfer equipment").

Regarding claims 196, 197, 222 and 223, Seidel (July 1996) does not teach using the artificial insemination sample within 17 or 10 or no more than 5 or no more than 9 hours of establishing the sample. However, Seidel (Jan 1996) teaches the importance of inseminating bovine soon after the sorting is completed and teaches methods of inseminating bovine within 9 hours of sorting the sperm. In the absence of a definition in the specification or claims for the phrase "no more than about 5 hours," this phrase is considered to be included by the "within 9 hours" of Seidel (Jan 1996). According, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the artificial insemination sample as soon as possible following the formation of the sample in order to have ensured the viability of the sample, thereby improving the overall effectiveness of the insemination procedure.

Regarding claim 202 and 213-216, Seidel (July 1996) does not specifically teach sorting the sperm into a collector having a cushion to protect the cells from impact with the collector. However, Seidel (Jan 1996) teaches sorting the cells into an extender containing homologous seminal plasma. Collection into such a medium would have cushioned the sperm cells from impact with the collector. Accordingly, modification of the method of Seidel (July 1996) so as to have sorted the sperm cells using the method of Seidel (Jan 1996) would have resulted in a method that provided the benefit of collecting the sperm cells into a container while cushioning the sperm cells from impact with the collector.

Regarding claims 208 and 221-227, Seidel (July 1996) does not teach staining the cells with a solution of 38uM stain and then concentrating the sperm. However,

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Rens (col. 5) teaches staining the sperm with 7.1 uM Hoechst 3342 dye per  $15 \times 10^6$  sperm for 40 min at 32°C, sorting the sperm cells and then concentrating the sperm cells. It is noted that the present claims do not specify the type of stain, the final concentration of stain, the number of sperm or the conditions for staining the sperm. However, at the time the invention was made the parameters which effect staining of sperm cells prior to sorting were well known in the art. Thereby, to have determined the optimum concentration of stain, depending on the quantity of sperm and the conditions (time, temp) of staining would have been obvious to one of ordinary skill in the art and well within the skill of the art. As discussed in MPEP 2144.05(b), "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)." Accordingly, it would have been obvious to one of ordinary skill in the art and well within the skill of the art to have selected the optimum concentration of stain depending on the concentration of sperm, and the conditions of staining, including to have selected the concentration of 38 uM content of stain, in order to have provided the most effective means for staining the sperm to allow for accurate sorting, while maintaining the integrity and viability of the sperm. Further, with respect to claim 216, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have established a collection container having stream matched physical

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characteristics in order to have provided the benefit of preserving the integrity of the sperm cells.

Regarding claims 214, the combined references do not specify the size of the collection container. However, it would have been well within the skill of the art at the time the invention was made to have selected a collection container of an appropriate width in order to have prevented damaging the sperm since Rens teaches the criticality of the dimensions of the sorting device and the orientation of the sperm within the sorting device in order to maintain sperm viability (see, for example, column 3).

Regarding claims 219-227, Seidel teaches using 2 or  $5 \times 10^5$  total sperm. This is considered to be no more than one million or 5 million sperm, and no more than 350,000 sperm.

Further regarding claims 219-217, the combined references do not teach operating the high speed cell sorter at 50 psi. However, methods for sorting sperm using high speed cell sorters were well known in the art at the time the invention was made and the parameters which would effect the sorting process were also well known, including the pressure used to operate the flow cytometer. To determine the optimum conditions for performing a method step is well within the skill of the art. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Aller, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the optimum conditions for operating the flow

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cytometer, and thereby to have operated the flow cytometer at at least 50 psi in order to have provided the most effective means for sorting the sperm.

Regarding claim 224, Seidel (July 1996) teaches inserting one half of the artificial insemination sample into each uterine horn.

Regarding claims 225 and 226, Seidel (July 1996) teaches inseminating the female bovine 12 hours after the detection of estrus, which constitutes “no more than about 26 hours following observed standing estrus.” Further, since the term “about” has not been defined by the specification and claims, “no more than about 6 hours” is considered to encompass 12 hours. Additionally, to the extent that “no more than about 6 hours” is intended to encompass less than 12 hours, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have inseminated the female bovine soon after estrus was detected, including within 5 hours of detecting estrus, to ensure the fertility of the female bovine, thereby improving the success of the artificial insemination method.

Regarding claim 227, Seidel (July 1996) does not teach cooling the sperm to 5°C. However, Seidel (Jan 1996) teaches sorting sperm and storing sperm during shipping at 5°C. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel (July 1996) so that when sperm was to be shipped, cooling the sperm to 5°C during shipping, in order to have ensured the viability of the sperm, thereby providing improving the effectiveness of the artificial insemination method.

7. Claims 190 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (July 1996) in view of Seidel (Jan 1996) and Rens, as applied above, and further in view of Seidel (1995; cited in the IDS).

The teachings of Seidel (July 1996), Seidel (Jan 1996) and Rens are presented above. In particular, Seidel (July 1996) teaches insemination deep into the uterine horn ipsilateral to the ovary. Seidel does not teach insemination both ipsi and contra-lateral within the uterine horns.

However, Seidel (1995) teaches ipsilateral and contra-lateral insemination of low dose semen into females. The reference teaches that pregnancy rates were nearly identical for ipsilateral and contra-lateral insemination.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel (1996) so as to have performed the insemination procedure by inserting the semen both ipsi and contra-lateral into the uterine horns because this would have provided an equally effective means for inseminating female bovine.

8. Claims 205-207 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (July 1996) in view of Seidel (Jan 1996) and Rens, and further in view of Seidel (Theriogenology (1994) 41: 168; cited in the IDS).

The teachings of Seidel (July and Jan1996) and Rens are presented above. The combined references do not teach superovulating the females prior to insemination.

Seidel (1994) teaches methods for stimulating superovulation in cows. In the method of Seidel, cows are treated twice a day at 12 hour intervals with injections of 6,

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6, 4, 4, 2, 2, 2, and 2 mg FSH and given three dosages of prostaglandin of 25 mg and 12.5 mg PGF-2-alpha on days 6 and 7, respectively, of FSH treatments. The superovulation treatment is initiated starting between days 9 and 14 of the estrous cycle.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel so as to performed the surgical insemination procedure on females that were superovulated and synchronized using the FSH/PGF-2-alpha treatment methods as disclosed by Seidel (1994) in order to have achieved the benefit of providing a more effective and convenient means of insemination since the females could then be inseminated at the most optimal time during estrous and the timing of the insemination procedure could be scheduled to correspond with the collection and sorting of sperm.

9 Claim 203 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (July 1996) in view of Seidel (Jan 1996) and Rens, as set forth above, and further in view of Rath (Theriogenology (1997) 47: 75-800; cited in the IDS) and Seidel (1995; cited in the IDS).

The teachings of Seidel (July and Jan 1996) and Rens are presented above. The combined references do not specify the solution into which the sperm cells are collected and thereby does not teach collecting the sorted sperm in a citrate solution containing about 6% egg yolk.

However, Rath (page 796) teaches collecting sex-sorted sperm into a collection media composed of TEST extender containing 2% hen egg yolk. Thus, Rath teaches

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the concept of collecting sperm sorted cells into a sperm extender medium.

Additionally, Seidel (1995) teaches extending sperm in Cornell Universal Extender which is known to contain citrate and egg yolk.

In view of the teachings of Rath and Seidel (1995), it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel (1996) so as to have collected the sperm in an extender comprising a citrate solution and egg yolk in order to have sorted the sperm into a medium that would help to preserve the sperm and/or which could be used for subsequently freezing of the sperm.

10. Claim 220 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (July 1996) in view of Seidel (Jan 1996) and Rens, as set forth above, and further in view of Wilhelm (Cryobiology. 1996. 33: 320-329; cited in the IDS).

Seidel (July and Jan 1996) and Rens do not teach applying the artificial insemination method to equine sperm.

However, Wilhelm teaches the use of equine sperm for the purpose of artificial insemination. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the method of Rens to the sorting of equine sperm in order to have provided an effective means for distinguishing between and collecting populations of X- and Y-chromosome bearing sperm useful for artificially inseminating equine. Further, Wilhelm does not teach the quantity of equine used for artificial insemination. However, since the parameters which effect artificial insemination of equine were known in the art at the time the invention was made, it would have been



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obvious to one of ordinary skill in the art and well within the skill of the art to have selected an optimum quantity of sperm, wherein said quantity would be less than 25 million so as to have provided the most effective sample for inseminating equine while keeping the number of sperm to be used for insemination at the lowest possible number given the constraints on how many sperm could be sorted per day and the cost of sorting. Additionally, the ordinary artisan would have recognized that the quantity of sperm could be modified in order to have provided the most appropriate sperm sample depending on how the sample would be used – i.e., depending on the amount of sperm present in the original sample, whether the samples would be frozen prior to use, the number of samples to be used for insemination, and the type of insemination technique. Accordingly, to have generated sorted sperm samples containing less than 25 million sperm and to have used the sperm samples for artificial insemination of equine would have been obvious to one of ordinary skill in the art because the ordinary artisan would have recognized that the quantity of sperm could be and should be optimized to enhance the efficiency of the artificial insemination, while providing the most economical means for achieving artificial insemination.

11. Claims 200 and 201 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (July 1996) in view of Seidel (Jan 1996), Rens and Wilhelm, and further in view of Catt (Reprod. Dom. Animal (1997). 32: 251-258; cited in the IDS).

The teachings of Seidel, Rens, and Wilhelm are presented above.

Seidel (July 1996) does not teach establishing a sheath fluid which contains a HEPES buffered medium or sodium citrate.

However, Catt teaches that semen may be diluted in a HEPES-buffered SOF (synthetic oviduct fluid) medium or a BTS solution containing sodium citrate and that such a fluids are suitable for maintaining the viability of spermatozoa (see, e.g., page 252 and 257). Catt also teaches that it is beneficial to sort into a medium containing a cushioning of seminal plasma to increase the viability and motility of sperm. Catt (page 256-257) teaches that while PBS is often used as a sheath fluid for sorting, it can be beneficial to include additional salts to the sheath fluid to increase the viability and motility of the sperm.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Seidel (July 1996) so as to have used a HEPES-buffered medium or a sodium citrate-containing medium for establishing a sheath fluid for sorting the sperm because Catt teaches that these solutions provide a suitable dilution medium for sperm and thereby using HEPES-buffered medium or a sodium-citrate containing solution as the sheath fluid would have achieved the benefit of ensuring the viability and motility of the sperm. Further, in the absence of evidence to the contrary, to have selected the optimum concentration of sodium-citrate, including 2.9%, based on the concentration and identity of other reagents in the sheath fluid would have been obvious to and well within the skill of the ordinary artisan at the time the invention was made.

**Response to remarks regarding the previous 103 rejections:**

In the response, Applicants traversed the previous grounds of rejection under 35 USC 103. Applicants state that Rens does not exemplify methods that explicitly disclose

sort rates of at least 1200 sorts per second. This argument has been fully considered but are not persuasive regarding claims 221-227 because these claims require only sort rates of 500 sorts/second.

Applicants state that the sort rate of Rens cannot be inferred. Applicants point to the Rens 1999 publication as showing that a cell sorter equipped with an elliptical nozzle provided sampling rates of 2000 sperm/second, resulting in sort rates of 200 sperm /second. It is argued that these sort rates are below those presently claimed. Applicants assert that the Office has not provided any evidence to establish that the Rens '216 patent achieved sort rates of 1200 sorts/second. Applicants assert that they are under no obligation to provide evidence of nonobviousness.

These arguments have also been fully considered but are not persuasive.

With respect to the Rens 1999 reference (Molecular Reproduction and Development 52: 50-56), the data disclosed therein was obtained using an EPICS 750 series flow cytometer equipped with an elliptical nozzle. In addition to Applicant's characterization of this reference, Rens (1999) also teaches that sampling rates of 3,000 to 4,000 have been achieved and that these sampling rates provide equally effective results as that obtained with sampling rates of 500 sperm/second (page 53). Rens (1999) also notes that the new elliptical nozzle has been fitted onto the MoFlo® high speed cell sorter and "even greater increases in sorting efficiency" have been achieved (page 55). It is this modified MoFlo® high speed sorter equipped with an elliptical nozzle that is disclosed in the Rens '216 patent, over which the present claims have been rejected (see, e.g., col. 5 of the '216 Rens patent). Rens (1999) does not

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state the particular sorting rates achieved with the modified MoFlo® sorter. However, Johnson (Animal Reproduction Science. 2000. 60 : 93-107) does discuss the improved sorting results obtained with the modified MoFlo® sorter equipped with the elliptical nozzle of Rens. In particular, Johnson (2000; page 98), teaches that this modified device has the capacity to sort at rates of 50,000 events/second, as compared to the standard rate of 5,000 to 10,000 events/ second. Johnson (2000; abstract) teaches that this modified MoFlo® sorter with an elliptical nozzle (i.e., the device disclosed by Rens '216) allows for the sorting of X-bearing sperm at a rate of about 18 million sperm / hour – i.e., 5000 sperm/sec.

Accordingly, given the analogy set forth by Applicants with respect to the Rens (1999) reference, if a sampling rate of 2000 sperm / second results in a sort rate of 200 sperm/second, then the sampling rate of 15,000 disclosed by the Rens '216 patent should achieve sort rates of 1,500 sperm/sec (see col. 4, lines 29-31 of '216). Thereby, in the absence of evidence to the contrary, it is maintained that such sampling rates would allow for sorting rates of at least 500 sorts/ second (claims 221-227) and 1,200 sorts/second.

Further, even if Rens does not specifically exemplify a method in which sort rates of 500 or 1,200 sorts/sec are achieved, Rens provides the motivation to use the modified MoFlo® flow cytometer to achieve the sorting and collection rate of at least 500 or 1,200 sperm / sec because Rens specifically teaches the need to obtain large quantities of sorted sperm in a short period of time to allow for successful artificial insemination of mammals with sorted sperm (col. 4, lines 43-49; col. 5, lines 46-57).

Applicants are reminded that that the present rejection is made under 35 USC 103, and not under 35 USC 102. Obviousness does not require absolute predictability but only the reasonable expectation of success. See In re Merck and Company Inc., 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986) and In re O'Farrell, 7 USPQ2d 1673 (Fed. Cir. 1988).

Additionally, as stated in *Ex parte Kubin* (No. 2007-0819, Bd. Pat. App. & Int. May 31, 2007): "Under *KSR*, it is now apparent "obvious to try" may be an appropriate test in more situations than we previously contemplated. When there is motivation to solve a problem and there are a finite number of identified predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under 103. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct 1727, 82 USPQ2d 1385, 1397 (2007)." This reasoning is also applicable to the present situation wherein the prior art of Rens provides both the motivation to increase the rate of sorting and collecting sperm and the means (i.e., the modified MoFlo® sorter equipped with the elliptical nozzle) to achieve the result of sorting and collection rates of about 500 sorts/second or 1,200 sorts/second.

**The following are new grounds of rejection necessitated by Applicants filing of a new patent applications and the amendments set forth therein:**

### **Double Patenting**

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225

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USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 186-194, 196,197, 199-203, 205-208, 210-216 and 219-226 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-123, 153-160 and 163-175 of U.S. Patent Application No. 11/536,492. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '492 are both drawn to methods for producing a nonhuman mammal wherein the methods comprise collecting sperm cells from a male, establishing a cell source which supplies sperm cells, sorting sperm cells so as to separate the sperm cells according to sex, inserting a portion of the sperm cells into a female and fertilizing at least one egg of said female. The present claims and the claims of '492 are both inclusive of methods wherein the nonhuman mammal is a bovine or equine. Further, the present claims and the claims of '492 are both inclusive of methods in which high speed flow cytometry is used to separate sperm cells at a rate of at least 1200 sorts/second. The instant claims and the claims of '492 also are inclusive of methods in which the sheath fluid contains a HEPES buffered medium, methods in which the sheath fluid comprises about 2.9% sodium citrate, methods in which sperm are stained using 38 uM

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of stain, methods in which a low dose of sperm cells is utilized, methods in which a chemically coordinated sheath fluid is used to create a sheath fluid environment for the sperm cells which is coordinated with both a pre-sort and post-sort sperm cell fluid environment, and methods in which the insemination sample is inserted both ipsi- and contra-lateral within the uterine horns of the female. Further regarding claims 219-216, the claims of '492 do not recite operating the high speed cell sorter at 50 psi. However, methods for sorting sperm using high speed cell sorters were well known in the art at the time the invention was made and the parameters which would effect the sorting process were also well known, including the pressure used to operate the flow cytometer. To determine the optimum conditions for performing a method step is well within the skill of the art. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Aller, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the optimum conditions for operating the flow cytometer, and thereby to have operated the flow cytometer at at least 50 psi in order to have provided the most effective means for sorting the sperm. Regarding claims 222 and 223, the claims of '492 recite inserting the artificial insemination sample no later than about 10 hours after establishing the artificial insemination sample. Because the term "about" has not been defined in the specification or claims, "no more than about 10 hours" is considered to include the recitation in the present claims of no more than about 5 hours. Regarding claim 224, the

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claims of '492 do not recite inseminating one half of the sample into each uterine horn. However, the claims of '492 do recite inserting a portion of the sample both ipsi- and contra-lateral within the uterine horns, and recite the quantity of sperm to be inserted. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method claimed in '492 so as to have inserted one half of the sample into each uterine horn in order to have provided an effective means for artificially inseminating the mammal. Regarding claims 225-226, the claims of '492 recite inseminating the female not later than 12 hours after the optimal time for performing artificial insemination, which is considered to include no more than about 6 or 26 hours after standing estrus is detected.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claim 227 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-123, 153-160 and 163-175 of U.S. Patent Application No. 11/536,492 in view of Seidel (Jan 1996).

Regarding claim 227, the claims of '492 do not recite cooling the sperm to 5°C. However, Seidel (Jan 1996) teaches sorting sperm and storing sperm during shipping at 5°C. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of claimed in '920 so that when sperm was to be shipped, cooling the sperm to 5°C during shipping, in order to have ensured the viability of the sperm, thereby providing improving the effectiveness of the artificial insemination method.



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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Carla Myers/

Primary Examiner, Art Unit 1634